IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

Appl. No.	: 10/596,876	Confirmation No.	: 1776
Applicant	: Smithey et al.	TC/A.U.	: 1618
Filed	: Nov. 28, 2006	Examiner	: BLESSING M FUBARA
Customer No.	: 152	Docket No.	: 0003.0551/PC32026A
Title	: SOLID COMPOSITIONS OF LOW-SOLUBILITY DRUGS AND POLOXAMERS		

APPEAL BRIEF

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April 25, 2011

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
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Real Party in Interest

The real party in interest by virtue of assignment is Bend Research, Inc., an Oregon corporation.

Related Appeals or Interferences

There are no related appeals or interferences.

Status of Claims

Claims 1-44, and 47-48 are cancelled. Claims 49-52 are withdrawn. Claims 45-46 and 53-62 are pending and stand rejected in a Final Rejection dated January 4, 2011 (although claim 53 is listed as being rejected in box 6 of the PTOL-326 form, no rejection of that claim is specified in the Detailed Action). A copy of the claims on appeal is set forth in the Claims Appendix.

Status of Amendments

All amendments, including the amendment after final dated January 25, 2011, have been entered.

Summary of Claimed Subject Matter

The sole independent claim 45 is directed to a pharmaceutical composition comprising a mixture that is not a molecular dispersion. Page 20, lines 2-5. The mixture has two components: (1) at least 50 wt% of particles comprise a low-solubility drug and a poloxamer (Page 11, lines 4-6), wherein at least 75 wt% of the drug is amorphous (Page 13, lines 9-11); and (2) a concentration-enhancing polymer. Page 19, lines 30-33.

Grounds of Rejection to be Reviewed on Appeal

There are two issues on appeal:

(1) whether claims 45-46, 54 and 57-62 are rendered obvious under 35 USC 103(a) by Infeld et al. WO 02/089835 (**Infeld**) in view of Beyerinck et al. US 6,763,607 (**Beyerinck**); and

(2) whether claims 45-46 and 54-62 are rendered obvious under §103(a) by the combination of Hoover et al. US 20010053778 (**Hoover**) and Babcock et al. US 20010053791 (**Babcock**).

ARGUMENT

Prior Art Relied Upon

Infeld discloses a pharmaceutical dosage form of amorphous nelfinavir mesylate and a poloxamer produced by a hot melt granulation process comprising blending the drug and the poloxamer, and heating the blend to a temperature lower than the decomposition temperature of the drug. This process results in granules of the drug embedded in the poloxamer. Other excipients can be included in the melt granulation. There is no disclosure of concentration-enhancing polymers, nor of compositions of (1) particles of drug and poloxamer, and (2) a concentration-enhancing polymer.

Beyerinck discloses a modified spray drying apparatus for making particles of a solid amorphous dispersion of a drug and a blend of a poloxamer and one or more of the five cellulosic polymers recited in appealed claim 46.

Hoover discloses compositions of glycogen phosphorylase inhibitors (GPIs). In pertinent part, the compositions may be simple physical mixtures of the GPIs and concentration-

enhancing polymers. Although many concentration-enhancing polymers are disclosed, poloxamers are not disclosed at all.

Babcock discloses compositions of a particular GPI. The compositions include amorphous drug mixed with a concentration-enhancing polymer. Babcock at [0096]. Poloxamers are disclosed as one of 107 examples of conventional formulation excipients for forming the compositions into tablets and the like. Babcock at [0125]-[0132]. There is no disclosure of compositions comprising (1) particles of amorphous drug and poloxamer, and (2) a concentration-enhancing polymer.

(1) Obviousness of Claims 45, 46, 54 and 57-62 over Infeld in view of Beyerinck

Claims 46, 54, and 57-62 all ultimately depend from claim 45. If claim 45 is not rendered obvious by the combination of Infeld and Beyerinck, then neither are claims 46, 54, and 57-62. *In re Fine*, 5 USPQ 2d 1596 (Fed Cir 1986).

In order to establish obviousness, the Office must establish motivation to modify a prior art reference to achieve the claimed invention and the rationale for such motivation must be clearly articulated. *KSR Int'l Co. v. Teleflex, Inc.*, 82 USPQ 2d 1385, 1396 (Sup Ct 2007).

As noted above, Infeld discloses dosage forms of amorphous drug and a poloxamer. Such compositions are formulated to provide a significant improvement in the dissolution rate of the dosage form while resulting in satisfactory bioavailability. Infeld, Page 4, lines 25-26. The Examiner contends that one of ordinary skill in the art would have been motivated to enhance the bioavailability and concentration of the Infeld amorphous drug by substituting a blend of enteric polymer and poloxamer taught by Beyerinck for poloxamer alone taught by Infled so as to further enhance the bioavailability of the Infeld drug. But Beyerinck specifically states that the product formed by his method is a dispersion of drug and polymer. Beyerinck at column 11, lines 20-24. Note that independent claim 45 is directed to a mixture that is not a dispersion. Since Beyerinck teaches away from the claimed invention, there is no motivation to combine it with Infeld to come up with the claimed subject matter.

(2) Obviousness of Claims 45, 46, and 54-62 over Hoover and Babcock

Claims 46, and 54-62 all ultimately depend from claim 45. If claim 45 is not rendered obvious by the combination of Hoover and Babcock, then neither are claims 46 or 54-62. *In re Fine, supra*.

As noted above, Hoover discloses mixtures of GPIs and concentration-enhancing polymers. The examiner concedes that Hoover does not disclose poloxamers (Final Rejection, page 7, paragraph 21), but relies on Babcock to supply this constituent. Focusing on one of the seven classes of excipients disclosed in paragraphs [0126]-[0132] of Babcock, totaling 107 excipients, the Examiner points to paragraph [0126] pertaining to "matrix materials, fillers or diluents" and picks out poloxamers, and from this contends that one of ordinary skill would be motivated to formulate a multi-layered tablet of a GPI, a concentration-enhancing polymer, a polysorbate for stabilizing the GPI, and a poloxamer. Final Rejection, pages 7-8, paragraph 23.

The examiner's rationale for the supposed motivation to pick one of 107 of Babcock's excipients (poloxamer) and combine it with the Hoover composition is that one of ordinary skill would expect the GPI's bioavailability to be improved. *Ibid*, page 8, paragraph 23, last two lines. But this rationale is not supported, given the teaching of Babcock that the 107 excipients set out in [0126]-[0132] are "customary formulation excipients" that "may be used for customary purposes and in typical amounts without adversely affecting the properties of the compositions." Babcock at [0125]. In other words, Babcock teaches that inclusion of any of his 107 excipients, including poloxamers, will not hurt the beneficial properties (such as bioavailability) of his GPI compositions so long as they are used in conventional ways known in the pharmaceutical arts. This scarcely amounts to a teaching or suggestion that inclusion of such excipients will improve bioavailability, as argued by the Examiner.

Additional Remarks

As noted in the Status of Claims section of this Brief, the Detailed Action portion of the Final Rejection did not reject claim 53. Since claim 53 is still pending, there is nothing of record as to why that claim is listed in the PTOL-326 as being rejected. However, it is submitted that claim 53 is novel and not obvious based on the prior art cited for the reasons stated above.

Conclusion

For the reasons stated, all of the rejections are submitted to be without merit, and should be reversed.

Respectfully submitted,

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CLAIMS APPENDIX

45. A pharmaceutical composition comprising a mixture that is not a molecular dispersion of the following components:

(1) at least 50 wt% of particles, said particles comprising a low-solubility drug and a poloxamer, wherein at least 75 wt% of said drug is amorphous; and

(2) a concentration-enhancing polymer.

46. The pharmaceutical composition of claim 45 wherein said concentration-enhancing polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, cellulose acetate trimellitate, carboxymethyl ethylcellulose, and mixtures thereof.

53. The composition of claim 45, wherein component (1) is a solid solution of said drug homogenously distributed throughout said poloxamer.

54. The composition of claim 45 or 53 wherein said mixture is a dry physical mixture.

55. The composition of claim 45 or 53 wherein components (1) and (2) of said mixture are present in different regions of said composition.

56. The composition of claim 55 wherein components (1) and (2) of said mixture are present in different layers of a multi-layer tablet.

57. The composition of claim 55 wherein said mixture is present in the same environment of use after components (1) and (2) have been co-administered to said environment of use at a time ranging from approximately the same time to within 60 minutes of each other.

58. The composition of claim 45 or 53 wherein said drug has a glass-transition temperature of at least 50°C.

59. The composition of claim 45 or 53 wherein said drug has a Log P value of greater than 6.5.

60. The composition of claim 45 or 53 wherein said drug has a melting point of T_m in K, and wherein said drug has a glass-transition temperature of $T_{g,drug}$ in K, and wherein the ratio of said melting point to said glass transition temperature, $T_m/T_{g,drug}$, is less than 1.4.

61. The composition of claim 45 or 53 wherein said ratio of said melting point to said glass-transition temperature, $T_m/T_{g,drug}$, is less than 1.35.

62. The composition of claim 45 or 53 wherein said ratio of said melting point to said glass-transition temperature, $T_m/T_{g,drug}$, is less than 1.3.

EVIDENCE APPENDIX

Not applicable.

RELATED PROCEEDINGS APPENDIX

Not applicable.